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Japanese Published Unexamined (Kokai) Patent Publication No. S52-102434; Publication Date: August 27, 1977; Application No. S51-54580; Application Date: May 12, 1976; Int. Cl.²: A61K 31/35; Inventor(s): Eiichi Fujita et al.; Applicant: Nippon Shinyaku Co., Ltd.; Japanese Title: Oridonin oyobi Rashiokaurin yori Naru Kouganzai (Carcinostatic Agent Being Comprised of Oridonin and Lasiokaurin)

Specification

1. Title of Invention

Carcinostatic Agent Being Comprised of Oridonin and Lasiokaurin

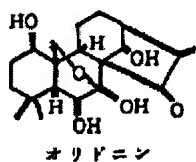
2. Claim

A carcinostatic agent that contains Oridonin and/or Lasiokaurin as effective components.

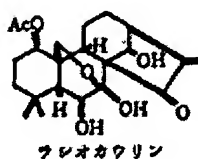
3. Detailed Description of the Invention

This invention pertains to a carcinostatic agent constituted having Oridonin and/or Lasiokaurin as effective components.

Oridonin and Lasiokaurin are diterpenoid bodies separated from Isodon plants of the Labiatae group, which have the following chemical structures:



Oridonin



Lasiokaurin

Oridonin and Lasiokaurin are described in detail as follow.

Oridonin is initially separated from the leaves of *Isodon japonicus* made in Kochi and demonstrates a melting point at 248 to 250°C (decomposition) and $[\alpha]_D -46^\circ$. Lasiokaurin is obtained from *Isodon lasiocarpus* made in Taiwan and demonstrates a melting point of 228 to 229°C and $[\alpha]_D -46^\circ$. The chemical structure and the absolute arrangement of these substances are determined by Fujita, one of the inventors, and others. Please refer to E. Fujita, et al., J. Chem. Soc., [C] 1970, 1674-1661 and E. Fujita, et al., Chem. Pharm. Bull., (Tokyo) 20 (8), 1752-1754 (19: 0).

Isodon lasiocarpus plants are used in public in the form of bitter stomachics from ancient times and show a significant effect particularly on stomachache. Nevertheless, a study on the effective constituents is hardly advanced.

During a study on a pharmacological effect of effective constituents of *Isodon lasiocarpus*, the inventors have unexpectedly found that Oridonin and Lasiokaurin demonstrate an extremely high carcinostatic effect, thereby attaining the invention. Pharmacological testing data on the carcinostatic effect of Oridonin and Lasiokaurin are indicated hereinbelow.

First, Oridonin or Lasiokaurin are dissolved in 20% ethanol. The solution is then injected into animals to test a carcinostatic effect.

ddY based male mice (20 ± 0.5 g average weight) are used for the animals. An Ehrlich ascitic cancer of 2×10^6 cells/mouse is inoculated within the abdominal cavities of these mice. The Oridonin or Lasiokaurin solution at 0.25 ml is then injected into the abdominal cavities 24 hours later. This injecting operation is applied total 7 times at every

24 hours. While the mice are observed for 40 days, the number of deaths is compared with that of the control so as to determine the carcinostatic effect of Oridonin and Lasiokaurin. The results are as follow. Note that the figures in the table are indicated based on the percentage in the number of surviving mice.

Table

Chemical substance to be dosed and the amount of dosage		Oridonin (Control)	Lasiokaurin (Control)
Days elapsed	[Please refer to the original description]		
Number of average days of survival		18.0 days / 32.4 days / 35.7 days / 17.1 days	30.4 days 17.6 days

As is clear in the testing results, at a dose of Oridonin at 10 mg/kg and 15 mg/kg to mice, the number of average days of survival is extended by 15.3 days for the 10 mg/kg dose and 18.6 days for the 15 mg/kg dose in comparison with those of the control group, which are equivalent to 60% and 70% life extending effects, respectively. At a dose of Lasiokaurin at 10 mg/kg as similarly to as above, the number of average days of survival is extended by 12.8 days, which is equivalent to a 40% life extending effect. On the other hand, according to an acute toxicity testing (a dose within the abdominal cavities) to mice, a 50% death ratio is 35 to 40 mg/kg at Oridonin and > 70 mg/kg at Lasiokaurin, which is larger than the aforementioned effective dosage. Thereby, Oridinin and Lasiokaurin of the invention are to be safe and effective carcinostatic agents.

As for the administration of these compounds to the human body, an oral administration, an injection and other methods are used. In the case of the oral administration, the compounds are formed into a powder agent or a tablet form using

lactose, starch and other appropriate non-toxic carriers. Or they can be sufficiently orally administered with a solution form, an emulsion or other forms. The dose at the time is adjusted as needed according to the symptoms and ages.

The compounds are dissolved in water as it is or after they have been converted into non-toxic salts to be used as injection solutions. An auxiliary dissolution substance can also be added if necessary. The obtained injection solution is injected by using a proper method such as an intramuscular injection or an intravenous injection. The dose is adjusted as needed according to the symptoms and ages. As described above, the invention offers a new and effective carcinostatic agent that demonstrates an excellent life extending effect on cancer patients.

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